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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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FAEGRE & BENSON LLP
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2200 WELLS FARGO CENTER
90 SOUTH 7TH STREET
MINNEAPOLIS, MN 55402-3901

EXAMINER	
TUNGATURTHI, PARITHOSH K	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 07/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/808,538	LEUNG ET AL.	
	Examiner	Art Unit	
	Parithosh K. Tungaturthi	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4 and 9-21* is/are pending in the application.

4a) Of the above claim(s) *15,16,18 and 19* is/are withdrawn from consideration.

5)☒ Claim(s) *20 and 21* is/are allowed.

6)☒ Claim(s) *3, 4 and 9-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11.15.04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 3, 4, 9-14, 20 and 21, in the reply of 04/28/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a)).

2. Claims 1-2, 5-8 and 17 are cancelled.

3. Claims 15, 16, 18 and 19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions.

4. Claims 3, 4, 9-14, 20 and 21 are under examination.

Specification

5. The disclosure is objected to because of the following informalities: The specification discloses the amino acid sequences of the CDRs of heavy and light chain regions (page 4 for example), however does not indicate the corresponding SEQ ID NOs of the CDRs. The applicant is requested to include the corresponding SEQ ID NO for each CDR in the specification.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 9-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9, 12 and 13 are indefinite for reciting "Gene". The instant claims are drawn to a isolated expression vector comprising a gene encoding for W12 heavy chain and a gene encoding for W12 light chain. According to Genes IV (Lewin et al, Oxford University Press, page 810, 1990), a gene is defined as "the segment of DNA involved in producing a polypeptide chain; it includes regions preceding and following the coding regions (leader and trailer) as well as intervening sequences (introns) between individual coding segments (exons)." From the teachings of the specification, however, the nucleic acid sequences encoding for the W12 light and heavy chains appear limited to the specific coding regions, and do not include expression control elements that fall under the definition of a gene. Accordingly, the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 3 and 4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding a chimeric anti-idiotype

antibody or fragment thereof, wherein said antibody or fragment thereof specifically binds to the idiotype region of an anti-CEA monoclonal antibody comprising all of the rW12 heavy and light chain variable regions as set forth in SEQ ID NOs:1, 2 and 3 and SEQ ID NOs:4, 5, and 6 respectively, does not reasonably provide enablement for an anti-idiotype antibody which does not contain a full set of six CDRs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to an isolated polynucleotide according to claim 20 or 21, comprising sequences encoding at least two rWI2 heavy chain CDRs, selected from the group of CDRs consisting of: the complementary determining region-1 (CDR-1) sequence NYWMT (SEQ ID NO:1), the complementary determining region-2 (CDR-2) sequence SITSTGGTYHAESVKG (SEQ ID NO:2), and the complementary determining region-3 (CDR-3) sequence DDYGGQSTYVMDA (SEQ ID NO:3) and an isolated polynucleotide according to claim 20 or 21, comprising sequences encoding at least two

rWI2 light chain CDRs, selected from the group of CDRs consisting of: the complementary determining region-1 (CDR1) sequence RASQDIGNYLR (SEQ ID NO:4), the complementary determining region-2 (CDR2) sequence GATNLAA (SEQ ID NO:5), and the complementary determining region-3 (CDR3) sequence LHHSEYPYT (SEQ ID NO:6).

The specification teaches a nucleic acid encoding a chimeric anti-idiotype antibody or fragment thereof, wherein said antibody or fragment thereof specifically binds to the idiotype region of an anti-CEA monoclonal antibody comprising all of the rW12 heavy and light chain variable regions as set forth in SEQ ID NOs:1, 2 and 3 and SEQ ID NOs:4, 5, and 6 respectively. The specification fails to enable an anti-idiotype antibody or fragment thereof which does not contain full set of six CDRs.

The claims are not commensurate in scope with the enablement provided in the specification. It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable

regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc. Natl. Acad. Sci. USA 1982 Vol 79 page 1979). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function.

It is unlikely that isolated polynucleotide, encoding at least two rW12 heavy chain CDRs or at least two rW12 light chain CDRs, as defined by the claims which may contain less that the full complement of CDRs from the heavy and light chain variable regions have the required binding function. The specification provides no direction or guidance regarding how to produce all the nucleic acid molecules as broadly defined by the claims. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

One of skill in the art would neither expect not predict the appropriate functioning of the antibody às broadly as is claimed.

10. Claims 9-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 9, 12 and 13 are drawn to an isolated expression vector comprising a first gene for the WI2 heavy chain and second gene for the WI2 light chain; an isolated first expression vector comprising a gene for W12 heavy chain and an isolated second expression vector comprising a gene for the W12 light chain; and an isolated first and second expression vectors, wherein said genes are for chimeric or humanized W12 light and heavy chain.

Thus, the instant claims are broadly drawn to a large genus of nucleic acid molecules and members of the genus are variable because of the potentially of the many different proteins they may encode. The specification teaches a rat anti-idiotypic antibody (rWI2) light chain variable region comprising SEQ ID NO:22 and heavy chain variable region comprising SEQ ID NO: 18 and the cDNAs encoding the specific amino acid sequence. As described above, a gene is defined as "the segment of DNA involved in producing a polypeptide chain; it includes regions preceding and following the coding regions (leader and trailer) as well as intervening sequences (introns) between individual coding segments (exons)." Therefore, many structurally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. Applicants' disclosure fails to describe any cDNAs that correspond to the W12 heavy and light chains, nor is it clear that the resulting sequences would be full-length. The sequence prepared from undefined parts of a cDNA clone may not comprise the entire coding region of any particular gene, nor is it clear that partial sequences would even be in frame to encode the W12 heavy and light chains. The claims, as written encompass polynucleotides, which vary substantially in length and

also in nucleotide composition. The specification does not contain any disclosure of the function of a full-length open reading frame (ORF) that includes the W12 heavy and light chains. Further, the specification does not describe any of the structural elements of a gene that would encode the sequences as claimed. For example, the specification does not describe the organization, location or actual DNA sequences of promoter and regulatory regions and introns, all defining elements of a "gene". The specification lacks information to lead on of skill in the art to understand that the applicant had possession of the broadly claimed invention at the time the instant application was filed. Thus, one of skill in the art would not understand that the applicant had possession of the claimed invention at the time the instant application was filed.

Conclusion

11. Claims 20 and 21 are found allowable.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

13. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Parithosh K. Tungaturthi, Ph.D.
Ph: (571) 272-8789

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER